

Application No. 09/493,480
Attorney Docket No. CRX113US

AMENDMENTS TO THE CLAIMS

In the Claims:

1-92. (canceled)

93. (Currently amended) An isolated nucleic acid molecule encoding a polypeptide comprising a ~~HER-2/Neu fusion protein, the HER-2/Neu fusion protein consisting of:~~

- (a) ~~HER-2/Neu extracellular domain linked to an amino acid sequence having at least 90% sequence identity to SEQ ID NO:3 and capable of producing an immune response against the HER-2/Neu extracellular domain in a warm-blooded animal; and~~
- (b) ~~a HER-2/Neu phosphorylation domain an amino acid sequence having at least 90% sequence identity to SEQ ID NO:4, and which increases the immunogenicity of (a) in a warm-blooded animal;~~

~~wherein (a) and (b) are joined by an amino acid linker sequence of no more than 50 amino acids; and wherein said polypeptide does not comprise and not comprising a HER-2/Neu transmembrane domain sequence or any portion of a HER-2/Neu intracellular domain other than the phosphorylation domain, wherein the HER-2/Neu fusion protein comprises at least 90% identity to SEQ ID NO:6 and wherein the HER-2/Neu fusion protein is capable of producing an immune response against a HER-2/Neu protein in a warm-blooded animal.~~

94.-97. (canceled)

98. (Currently amended) A viral vector comprising a nucleic acid molecule of claim 93.

99. (Currently amended) A composition comprising the nucleic acid molecule of claim 93, and a physiologically acceptable carrier or diluent.

100. (previously presented) The composition of claim 99, wherein the composition is a vaccine.

Application No. 09/493,480
Attorney Docket No. CRXII13US

101. (previously presented) The composition of claim 99, further comprising an immunostimulatory substance.

102. (currently amended) The composition of claim 99, wherein the nucleic acid molecule is a DNA molecule.

103. (Currently amended) An isolated nucleic acid molecule encoding a polypeptide comprising a ~~HER-2/Neu fusion protein, the HER-2/Neu fusion protein consisting of:~~

(a) ~~a HER-2/Neu extracellular domain and linked to an amino acid sequence having at least 90% identity to SEQ ID NO:3 and capable of producing an immune response against the HER-2/Neu extracellular domain in a warm-blooded animal; and~~

(b) ~~a fragment of the HER-2/Neu phosphorylation domain, an amino acid sequence having at least 90% identity to SEQ ID NO: 5, and that increases the immunogenicity of (a) in a warm-blooded animal;~~

~~wherein (a) and (b) are joined by an amino acid linker sequence of no more than 50 amino acids; and wherein said polypeptide does not comprise, and not comprising a HER-2/Neu transmembrane domain sequence or any portion of a HER-2/Neu intracellular domain other than the fragment of the phosphorylation domain, wherein the HER-2/Neu fusion protein comprises at least 90% identity to SEQ ID NO:7 and wherein the protein is capable of producing an immune response against a HER-2/Neu protein in a warm-blooded animal.~~

104. -107. (Cancelled)

108. (Currently amended) A viral vector comprising a nucleic acid molecule of claim 103.

109. (Currently amended) A composition comprising the nucleic acid molecule of claim 103, and a physiologically acceptable carrier or diluent.

Application No. 09/493,480
Attorney Docket No. CRX113US

110. (previously presented) The composition of claim 109, wherein the composition is a vaccine.

111. (previously presented) The composition of claim 109, further comprising an immunostimulatory substance.

112. (Currently amended) The composition of claim 109, wherein the nucleic acid molecule is a DNA molecule.

113. (Currently amended) A method of making a ~~fusion~~ protein, the method comprising the steps of:

- (a) introducing into a cell an expression vector comprising a nucleic acid molecule according to claims 93 or 103;
- (b) culturing the transfected cell; and
- (c) purifying the expressed ~~fusion~~ protein.

114. (Original) The method of claim 113, wherein the cell is a CHO cell.

115. (Original) The method of claim 113, wherein the cell is cultured in suspension, under serum-free conditions.

116. (Currently amended) The method of claim 113, wherein the expressed ~~fusion~~ protein is purified by a ~~two-step procedure~~, the procedure comprising:

- (a) anion exchange chromatography; and
- (b) hydrophobic chromatography.

117. (Currently amended) The nucleic acid molecule of claim 93, wherein (a) consists of the ~~HER-2/Neu fusion protein consists of an amino acid sequence of SEQ ID NO:3 and~~ (b) consists of ~~linked to an amino acid sequence of SEQ ID NO:4.~~

Application No. 09/493,480
Attorney Docket No. CRX113US

118. (Currently amended) The nucleic acid molecule of claim 103, wherein (a) consists of 93, ~~wherein the HER-2/Neu fusion protein consists of an amino acid sequence of SEQ ID NO:3 and (b) consists of~~ linked to an amino acid sequence of SEQ ID NO:5.

119. (Currently Amended) ~~The nucleic acid of claim 117, An isolated nucleic acid molecule encoding a polypeptide comprising wherein the HER-2/Neu fusion protein consists of an amino acid of SEQ ID NO:6.~~

120. (Currently Amended) ~~The nucleic acid of claim 118, An isolated nucleic acid molecule encoding a polypeptide comprising wherein the HER-2/Neu fusion protein consists of an amino acid sequence of SEQ ID NO:7.~~

121. (Currently amended) The nucleic acid molecule of claim 93, wherein the polypeptide is secreted.

122. -123. Canceled

124. (Currently amended) The nucleic acid molecule of claim 103, wherein the polypeptide is secreted.

125. (Previously presented) The composition of claim 109, comprising an oil-in-water emulsion.

126. (Previously presented) The composition of claim 125, comprising tocopherol.

127. (Previously presented) The composition of claim 111, wherein the immunostimulatory substance comprises 3D-MPL, QS21, or a combination of 3D-MPL and QS21.

128. (Previously presented) The composition of claim 111, wherein the immunostimulatory substance comprises 3D-MPL and QS21 in an oil-in-water emulsion.

Application No. 09/493,480
Attorney Docket No. CRX113US

129. (Previously presented) The composition of claim 128, comprising tocopherol.
130. (Previously presented) The composition of claim 109, comprising a CpG-containing oligonucleotide.
131. (New) An isolated nucleic acid molecule encoding a polypeptide comprising:
 - (a) a sequence having at least 90% sequence identity to SEQ ID NO:3 and capable of producing an immune response against the human HER-2/Neu extracellular domain in a warm-blooded animal; and
 - (b) a sequence having at least 90% sequence identity to SEQ ID NO:4, and which increases the immunogenicity of (a) in a warm-blooded animal;wherein the sequences of (a) and (b) are directly linked via a peptide bond.
132. (New) A viral vector comprising a nucleic acid molecule of claim 131.
133. (New) A composition comprising the nucleic acid molecule of claim 131 and a physiologically acceptable carrier or diluent.
134. (New) The composition of claim 133, wherein the composition is a vaccine.
135. (New) The composition of claim 133, further comprising an immunostimulatory substance.
136. (New) The composition of claim 133, wherein the nucleic acid molecule is a DNA molecule.
137. (New) The nucleic acid molecule of claim 131, wherein the polypeptide is secreted.
138. (New) The composition of claim 133, comprising an oil-in-water emulsion.

Application No. 09/493,480
Attorney Docket No. CRX113US

139. (New) The composition of claim 135, wherein the immunostimulatory substance comprises 3D-MPL, QS21, or a combination of 3D-MPL and QS21.

140. (New) The composition of claim 133, further comprising a CpG-containing oligonucleotide.

141. (New) An isolated nucleic acid molecule encoding a polypeptide comprising:
(c) a sequence having at least 90% sequence identity to SEQ ID NO:3 and capable of producing an immune response against the human HER-2/Ncu extracellular domain in a warm-blooded animal; and
(d) a sequence having at least 90% sequence identity to SEQ ID NO:5, and which increases the immunogenicity of (a) in a warm-blooded animal;
wherein the sequences of (a) and (b) are directly linked via a peptide bond.

142. (New) A viral vector comprising a nucleic acid molecule of claim 141.

143. (New) A composition comprising the nucleic acid molecule of claim 141 and a physiologically acceptable carrier or diluent.

144. (New) The composition of claim 143, wherein the composition is a vaccine.

145. (New) The composition of claim 143, further comprising an immunostimulatory substance.

146. (New) The composition of claim 143, wherein the nucleic acid molecule is a DNA molecule.

147. (New) The nucleic acid molecule of claim 141, wherein the polypeptide is secreted.

148. (New) The composition of claim 143, comprising an oil-in-water emulsion.

Application No. 09/493,480
Attorney Docket No. CRX113US

149. (New) The composition of claim 145, wherein the immunostimulatory substance comprises 3D-MPL, QS21, or a combination of 3D-MPL and QS21.

150. (New) The composition of claim 143, further comprising a CpG-containing oligonucleotide.

151. (New) A method of making a protein, the method comprising the steps of:

- (a) introducing into a cell an expression vector comprising a nucleic acid molecule according to claim 131 or claim 141;
- (b) culturing the transfected cell; and
- (c) purifying the expressed protein.

152. (New) The method of claim 151, wherein the cell is a CHO cell.

153. (New) The method of claim 151, wherein the cell is cultured in suspension, under serum-free conditions.

154. (New) The method of claim 151, wherein the expressed protein is purified by a procedure comprising:

- (a) anion exchange chromatography; and
- (b) hydrophobic chromatography.

155. (New) The composition of claim 99, comprising an oil-in-water emulsion.

156. (New) The composition of claim 101, wherein the immunostimulatory substance comprises 3D-MPL, QS21, or a combination of 3D-MPL and QS21.

157. (New) The composition of claim 99, further comprising a CpG-containing oligonucleotide.